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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,566	12/12/2001	Naohiro Takemoto	033025-002	4857

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EXAMINER	
COPPINS, JANET L	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,566	TAKEMOTO ET AL.	
	Examiner	Art Unit	
	Janet Coppins	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 22-49* is/are pending in the application.

4a) Of the above claim(s) *25-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 and 22-49 pending in the instant application.

Election/Restrictions

1. Pursuant to Applicants' election, the Group and/or Art Unit of the instant application in the PTO has changed. To aid in correlating any papers for the application, all further correspondence regarding this application should be directed to group Art Unit 1625.

2. Applicant's election with traverse of Group III, compounds and pharmaceutical compositions according to formula (I) wherein E^2 is nitrogen, in the Response of December 2, 2003, is acknowledged. The traversal is on the grounds that:

(a) Applicants allege that since the instant application was filed under §371, the "unity of invention standard" for determining restriction should be used, and that "unity of invention" exists in the instant case.

(b) Applicants also contend that restriction is proper only when there is a serious burden on the Examiner to examine all the claims in a single application, and that in the present application, since there is a close relationship between the subject matter of the ten sets of claims, there would be no serious burden on the Examiner to examine all of the claims.

3. This is not found persuasive because:

Regarding (a) above, Examiner Gucker had determined that a lack of unity of invention existed, as defined in Rule 13:

PCT Rule 13.1 states that the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention").

PCT Rule 13.2 states that unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.

Annex B, Part 1(a), indicates that the application should relate to only one invention, or if there is more than one invention, inclusion is permitted if they are so linked to form a single general inventive concept.

Annex B, Part 1(b), indicates that "special technical features" means those technical features, which as a whole define a contribution over the prior art.

Annex B, Part 1(f) indicates the "Markush practice" of alternatives in a single claim. Part 1(f(i)) indicates the technical interrelationship and the same or corresponding special technical feature is considered to be met when: (A) all alternatives have a common property or activity, and (B) a common structure is present or all alternatives belong to a recognized class of chemical compounds. Further defining (B) in Annex B, Part 1(f)(i-iii), the common structure must; a) occupy a large portion of their structure, or b) the common structure constitutes a structurally distinctive portion, or c) where the structures are equivalent and therefore a recognized class of chemical compounds, each member could be substituted for one another with the same intended result. That is, with a common or equivalent structure, there is an expectation from knowledge in the art that all members will behave in the same way. Thus, the technical relationship and the corresponding special technical feature result from a common (or equivalent) structure that is

responsible for the common activity (or property). Part 1(f(iv)) indicates that when all alternatives of a Markush grouping can be differently classified, it shall not, taken alone, be considered justification for finding a lack of unity. Part 1(f(v)) indicates that when dealing with alternatives, it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention shall be reconsidered, but does not imply that an objection shall be raised.

As stated in the previous Office Action, the claims lack unity of invention under PCT Rule 13.1 and 13.2, since the compounds defined in the claims lack a significant structural element, qualifying as the special technical feature that defines a contribution over the prior art. The compounds claimed in Groups I-X contain an aminophenyl-acetamide-piperidine backbone, which does not define a contribution over the prior art. Furthermore, the substituents pertaining to the "Q" moiety vary from a lower alkyl group to a substituted heteroaryl group, and when taken as a whole result in vastly different compounds. Each of the groups set forth in the previous Office Action represents a separate process or discrete heterocyclic ring system, which aside from sharing no significant structural element, cannot be said to belong to a recognized class of chemical compounds. These inventions are distinct from one another because they have achieved a separate status in the art, and require searches that are not coextensive, and are capable of supporting separate patents. Furthermore, no significant structural element exists, since the technical feature of the aminophenyl-acetamide-piperidine linkage (variables not being considered) exists in the prior art, please refer to CAS RN 264904-01-0, for example, of U.S. Pat. No. 6,559,146. Accordingly, the unity of invention is considered to be lacking and

restriction of the invention in accordance with the rules of unity of invention is considered to be proper.

Regarding (b) above, the Examiner would like to point out that "burden of search" is not part of the criteria used for determining lack of unity in applications filed under §371, please refer to MPEP 1893.03(d).

The requirement is still deemed proper and is therefore made FINAL.

4. Accordingly, claims 25-49 withdrawn from further consideration, as well as compounds and compositions according to formula (I) wherein E^2 is oxygen, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the Response of December 2, 2003.

5. This application contains claims 25-49 drawn to an invention non-elected with traverse. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

6. Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

7. Receipt is acknowledged of Applicants' Information Disclosure Statements, submitted December 12, 2001,and July 26, 2002, which are in compliance with 37 CFR 1.97. Accordingly, the Information Disclosure Statements have been considered by the Examiner and entered of record in the file.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-3 and 22-24 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,559,146. Although the conflicting claims are not identical, they are not patentably distinct from each other, because formula (I) of the instant application significantly overlaps with claimed formula (I), recited in the '146 patent. It would have been prima facie obvious to one of ordinary skill in the art at the time of filing the instant application to modify the thyroid receptor ligand of the '146 patent, employing a nitrogen for the E^2 variable. The above compound is specifically described in Table 1 found in the '146 patent, which teaches preferred embodiments of the reference patent's

general formula I, which also read on the instant application, (i.e. the instant claims are directed to species of aminophenyl-acetamide piperidine compounds wherein Q is preferably hydrogen phenyl, pyridyl, quinolyl, isoquinolyl, benzimidazole, please refer to page 6 of the specification). One of skill in the art would have recognized that both the '146 patent and the instant claimed compounds have the same utility, neuroprotective compounds that are useful for treating cerebral functional disorders. Therefore one skilled in the art would have been motivated to employ the genus compounds of general formula I of the '146 patent with the expectation of obtaining a similar genus of aminophenyl-acetamide compounds, that possess the same activity and are useful for the same utility.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-3 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds according to formula (I) wherein Q' is hydrogen or certain cyclic groups, does not reasonably provide enablement for compounds wherein Q' is any or all cyclic, aryl, or heteroaryl group. In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,

7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, applicants are claiming an aminophenyl-acetamide compound according to formula (I). The nature of the invention is of a compound of claim 1, which has neuroprotective ability. As stated, however, the claim broadly recites that any or all cyclic moieties are intended for the Q' variable. In order to practice the claimed invention, one skilled in the art would have to screen numerous cyclic groups to see which ones would work for the purposes stated in the present invention. However, the large number of groups embraced by the terminologies used in the claims (i.e., cyclic group, aryl group, heteroaryl group, cyclic hydrocarbon group, heterocyclic group, etc.) that would have to be screened imposes undue experimentation on the skilled artworker. Because the current claims do not provide sufficient guidance to one of ordinary skill in the art as to the vast number of cyclic groups that are generically recited, the quantity of experimentation for such a claim is considered to be undue. Therefore, the broad terminologies indicated above are not enabled. The Examiner suggests incorporating some of the cyclic groups that Applicants are enabled for, such as the preferred groups listed on page 6 of the specification, i.e. phenyl, pyridyl, quinolyl, isoquinolyl, benzothiazole, and benzimidazole.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

> subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1-3 and 22-24 rejected under 35 U.S.C. 102(e) as being anticipated by Annoura, Hirokazu et al U.S. Pat. No. 6,559,146. The '146 patent discloses and recites aminophenoxyacetic acid derivatives according to formula (I) of column 2, and preferred compounds listed in Examples 18-27, 40, 41, 70, 76, 78, 88, 94, and 109-139, and the corresponding examples in Table 1, which read directly on the elected species of compounds of the instant invention (compounds wherein E_2= nitrogen).

The applied reference has common assignee/inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1-3 and 22-24 rejected under 35 U.S.C. 103(a) as being obvious over Annoura, Hirokazu U.S. 6,559,146.

The applied reference has common assignee/inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in

accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicant is claiming the following compound and process:

Neuroprotective compounds consisting of an aminophenyl-acetamide piperidine structure, and pharmaceutical compositions containing them, for treating functional disorders of the brain.

Determination of the scope and content of the prior art (MPEP §2141.01)

The '146 patent teaches and recites aminophenyl-acetamide piperidine derivatives according to formula (I) in column 2 and preferred compounds of Table 1, including compounds wherein E^2 is nitrogen. The '146 patent also discloses and recites pharmaceutical compositions, for use in the treatment of cerebral functional and organic disorders.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The compounds of the instant invention and the conflicting claims of the reference patent differ in that the formula of instant claim 1 is not identical to the recited formula in claim 1 of the '146 patent, since the instant claim 1 overlaps the subject matter of the reference patent.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

To those skilled in chemical art, the instant elected group of aminophenyl-acetamide compounds is not such an advance over the genus of compounds previously patented in the '146 reference, as requires invention, because chemists knowing the neuroprotective properties of the

aminophenyl-acetamide compounds already patented would know what to expect in a genus of compounds that overlaps the patented compounds. The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare the compounds taught in the reference with the expectation of obtaining compounds which could be used for treating the same cerebral functional disorders. It would have been prima facie obvious to employ the formula claim 1 of the '146 patent, particularly when Applicants' elected Group III, compounds wherein E^2 is nitrogen, are taught as preferred compounds and specifically claimed in the reference patent, (i.e. the instant claims are directed to the same species of aminophenyl-acetamide piperidine compounds of the '146 patent wherein Q is preferably hydrogen phenyl, pyridyl, quinolyl, isoquinolyl, benzimidazole, please refer to page 6 of the instant specification).

Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Joseph McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
February 16, 2004

for

Joseph McKane, acting SPE
Art Unit 1625